Docket No.: 511582000100
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Aya JAKOBOVITS et al.

Application No.: 09/771,312

Art Unit: 1642

Filed: January 26, 2001

Examiner: B. Fetterolf

For: 84P2A9: A PROPSTATE AND TESTIS SPECIFIC PROTEIN HIGHLY EXPRESSED IN PROSTATE CANCER

DECLARATION OF KAREN JANE MEYRICK MORRISON
UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Karen Jane Meyrick MORRISON, declare as follows:

1. I have a Ph.D. in Pathology from The University of Southampton, U.K. I have worked in the field of histopathology and immunohistochemistry for nearly 25 years. A copy of my *curriculum vitae* is attached as Exhibit A.

2. I hold the position of Research Scientist III at Agensys, Inc., and I supervise the tissue analysis facility and staff. I carry out all procedures associated with histology, including the preparation, processing, cutting, staining, and analysis of samples by histological, histochemical and immunohistochemical techniques. These activities include analysis of tissues and cells by bright field microscopy, fluorescence microscopy and computer-aided systems.

3. We tested the expression of 84P2A9 protein by immunohistochemistry in tumor specimens of prostate cancer and lung cancer. Formalin fixed, paraffin wax-embedded tissues were cut into 4 micron sections and mounted on glass slides. The sections were de-waxed, rehydrated and treated with antigen retrieval solution (AR-10: BioGenex, San Ramon, California) at high temperature. Sections were then incubated in polyclonal rabbit anti-84P2A9 antibody for 3 hours. The slides were washed three times in buffer and further incubated with DAKO EnVision+™ peroxidase-conjugated goat anti-rabbit immunoglobulin secondary antibody (DAKO Corporation, Carpentaria, CA) for 1 hour. The sections were then washed in buffer, developed using the DAB kit (SIGMA Chemicals), nuclei are stained using hematoxylin, and analyzed by bright field microscopy. The cells which contain antigen immunoreactive with the 84P2A9 antibody stain brown.

Exhibit B shows two panels showing a prostate cancer specimen. Panel A shows a prostate cancer specimen treated with the antibody indicating strong expression of 84P2A9 protein in the tumor cells (brown coloration). Expression of 84P2A9 protein was detected both within the cytoplasm of the tumor cells and on the cell surface indicating that 84P2A9 protein is membrane associated in prostate cancer. Panel B shows an adjacent section of the prostate cancer specimen with the antibody directed to 84P2A9 protein omitted from the treatment, showing no brown staining. Blue coloration is hematoxylin, a nuclear stain.

4. We also used the same antibodies and the same staining protocol set forth in the previous paragraph to monitor protein expression in lung cancer. As described in the previous

paragraph, formalin fixed, paraffin wax-embedded tissues were cut into 4 micron sections and mounted on glass slides, de-waxed, rehydrated and treated with antigen retrieval solution at high temperature. The same antibody detection system as described above was employed; therefore, a brown stain indicates the presence of the antigen.

Exhibit C shows two panels showing a lung cancer specimen. Panel A shows a lung cancer specimen treated with the antibody and showed strong expression of 84P2A9 protein in the tumor cells (brown coloration). Expression of 84P2A9 protein was detected both within the cytoplasm of the tumor cells and on the cell surface indicating that 84P2A9 protein is membrane associated in lung cancer. Panel B shows an adjacent section of the lung cancer specimen with the antibody directed to 84P2A9 protein omitted from the treatment, showing no brown staining. Blue coloration is hematoxylin, a nuclear stain.

5. In my expert opinion, the results above clearly show that:

(i) 84P2A9 protein is produced in prostate cancer and can be detected by immunohistochemistry as set forth in the specification and confirmed by the protocols set forth above.

(ii) 84P2A9 protein is produced in lung cancer and can be detected by immunohistochemistry as set forth in the specification and confirmed by the protocols set forth above.

(iii) As a general matter, as set forth in the specification, the level of expression of 84P2A9 is higher in cancer tissue than in normal tissue.

6. In summary, in view of the specification and confirmation shown in the attached Exhibits, it is apparent that 84P2A9 protein can be used to elicit the production of antibodies immunoreactive with 84P2A9 protein and the 84P2A9 protein is useful in detecting the presence of cancer.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at Santa Monica, California, on this 07 of October 2005.

Karen Jane Meyrick Morrison

Exhibit A

CURRICULUM VITAE:

KAREN JANE MEYRICK MORRISON

CURRENT RESPONSIBILITIES:

Group Leader of Tissue Analysis Group.

Responsible for all histopathology including:

Immunohistochemistry: Identification and evaluation of antibodies produced to company's proprietary targets.

Tumor models: Assessment of 'in vivo' models by histological and immunohistochemical methods.

TRAINING/QUALIFICATIONS:

1998	PhD., Department of Pathology, University of Southampton, U.K. Title of thesis: An investigation of inflammatory cells in asthma as studied by immunohistochemical techniques on bronchial biopsies.
1985	Fellow, Institute of Biomedical Sciences, U.K.
1979	Associate, Institute of Biomedical Sciences, U.K.
1978	BSc. (Hons.) 2.2 Zoology, University of Southampton, U.K.

I. EMPLOYMENT

PRESENT EMPLOYMENT:

April 2001 – present	Research Scientist III, Agensys, Inc., 1545 Seventeenth Street, Santa Monica, CA 90404.

PREVIOUS EMPLOYMENT:

July 1994 - **January 2001**	B.M.S. 3 (Biomedical Scientist 3), Cardiothoracic Surgery, Imperial College School of Medicine at Harefield Hospital, Harefield, U.K.
September 1993 - **July 1994**	Research Associate, Smooth Muscle Group, U.M.D.S., St. Thomas's Hospital, London, U.K.
June 1992 - **August 1993**	Research Associate, Department of Medicine, University of Southampton at Southampton General Hospital, Southampton, U.K.

October 1988 - May 1992	Research Assistant, Department of Medicine, University of Southampton at Southampton General Hospital, Southampton, U.K.
September 1987 - October 1988	B.M.S. 2, Department of Histopathology, Royal Victoria Hospital, Boscombe, Bournemouth, U.K.
January 1986 - September 1987	B.M.S. 2, Department of Pathology, University of Southampton at Southampton General Hospital, Southampton, U.K.
November 1979 - January 1986	B.M.S. 1, Department of Pathology, University of Southampton at Southampton General Hospital, Southampton, U.K.
July 1978 - November 1979	Junior 'B' B.M.S., Department of Pathology, University of Southampton at Southampton General Hospital, Southampton, U.K.

EXPERIENCE:

- General histology. All general histological techniques including the sample preparation, processing, cutting and staining of sections from a variety of frozen, paraffin and resin embedded tissue.
- Immunohistochemistry. Extensive knowledge of numerous immunohistochemical techniques in a variety of tissue and cell preparations. These include the development and adaptation of various methods in frozen, paraffin and resin embedded preparations.
- Quantitative techniques. Methods for the evaluation of cells and tissue sections using both manual and computer-aided systems.
- In situ hybridisation. The use of non-radiolabeled techniques for the demonstration of mRNA in tissue sections.
- Responsibility. Instrumental in the establishment and day to day running of immunohistochemistry and general histology units previously for the Department of Medicine, Southampton General Hospital; Smooth Muscle Group, St Thomas's Hospital and Department of Cardiothoracic Surgery, Imperial College at Harefield Hospital and in the current post
- Training and supervision. The training and supervision of undergraduate and PhD students, biomedical scientists, academic research staff and clinicians undertaking projects requiring histological techniques. Teaching immunohistochemistry to visitors from other research institutions both in the U.K. and abroad.

1.

- Computer literacy. Literate in a broad spectrum of software including Office, image analysis and statistical packages.

KAREN JANE MEYRICK MORRISON

PUBLICATIONS:

Judd MA and **Britten (now Morrison) KJM**. (1982) Tissue preparation for the demonstration of surface antigens by immunoperoxidase techniques. Histochemical Journal 14: 747 - 753.

Stratford N, **Britten KJM** and Gallagher PJ. (1985) Inflammatory infiltrates in human coronary atherosclerosis. Atherosclerosis 59: 271 - 276.

Jones DB, **Britten KJM**, de Sousa M and Wright DH. (1985) The distribution of ferritin and ferric iron in the spleens of lymphoma patients and controls. In: Proteins of the Biological Fluids, Volume 32. Eds: H Reefers. Pergamon Press: Oxford.

Jones DB, **Britten KJM** and Wright DH. (1986) The staining of a panel of routine diagnostic tissue biopsies with workshop 'L' series antibodies. In: Leucocyte typing, Volume 2, Chapter 24. Eds; Reinherz and Nadler. Springer-Verlag: Berlin.

Britten KJM, Jones DB, de Sousa M and Wright DH. (1986) The distribution of iron and iron binding proteins in spleen with reference to Hodgkin's disease. British Journal of Cancer 54: 277 - 286.

Mepham BL and **Britten KJM**. (1990) Immunocytochemical techniques in lymphoreticular pathology. In: Lymphoproliferative Diseases, Chapter 12. Eds: Jones and Wright. Kluver Academic Publishers: London.

Djukanovic R, Wilson JW, **Britten KJM**, Wilson SJ, Walls AF, Roche WR, Howarth PH and Holgate ST. (1990) Quantitation of mast cells and eosinophils in the bronchial mucosa of symptomatic atopic asthmatics and healthy control subjects using immunohistochemistry. American Review of Respiratory Disease 142: 863 - 871.

Holgate ST, Djukanovic R, Wilson JW, Roche WR, **Britten KJM** and Howarth PH. (1991) Allergic inflammation and its pharmacological modulation in asthma. International Archives of Allergy and Applied Immunology 94: 210 - 217.

Howarth PH, Wilson JW, Djukanovic R, Wilson SJ, **Britten KJM**, Walls AF, Roche WR and Holgate ST. (1991) Airway inflammation and atopic asthma: a comparative bronchoscopic investigation. International Archives of Allergy and Applied Immunology 94: 266 - 269.

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Montefort S, Roche WR, Howarth PH, Djukanovic R, Gratziou C, Carroll MP, Smith L, **Britten KJM**, Haskard DO, Lee TH and Holgate ST (1992). Intracellular adhesion molecule-1 (ICAM-1) and endothelial leucocyte adhesion molecule-1 (ELAM-1) expression in the bronchial mucosa of normal and asthmatic subjects. European Respiratory Journal 5: 815 - 823.

Bradding P, Feather IH, Howarth PH, Mueller R, Roberts JA, **Britten KJM**, Bews JPA, Hunt TC, Okayama Y, Heusser CH, Bullock GR, Church MK and Holgate ST. (1992) Interleukin 4 is localised to and released by human mast cells. Journal of Experimental Medicine 176: 1381 - 1386.

Britten KJM, Howarth PH and Roche WR. (1993) Immunohistochemistry on resin sections. A comparison of resin embedding techniques for small mucosal biopsies. Biotechnic and Histochemistry 68: 271 - 280.

Bradding P, Roberts JA, **Britten KJM**, Montefort S, Djukanovic R, Mueller R, Heusser CH, Howarth PH and Holgate ST. (1994) Interleukins 4, 5 and 6 and tumour necrosis factor α in normal and asthmatic airways: evidence for the human mast cell as an important source of these cytokines. American Journal of Respiratory Cell and Molecular Biology 10: 471 - 480.

Amrani M, Latif N, **Morrison K**, Jayakumar N, Goodwin A, Gray C, Dunn M and Yacoub M. (1998) Relative induction of heat shock protein (HSP70) in coronary endothelial cells versus cardiomyocytes. Implications for myocardial protection. Journal of Thoracic and Cardiovascular Surgery 115: 200 - 209.

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Allen S, Dashwood M, **Morrison K** and Yacoub MH. (1998) Differential leukotriene constrictor responses in human atherosclerotic coronary arteries. Circulation 97: 2406 - 2413.

Borland JA, Chester AH, **Morrison KJM** and Yacoub MH. (1998) Alternative pathways of angiotensin II production in the human saphenous vein. British Journal of Pharmacology
125: 423 - 428.

Chester AH, **Morrison KJM** and Yacoub MH. (1998) Expression of vascular adhesion molecules in saphenous vein coronary bypass grafts. Annals of Thoracic Surgery 65: 1685 - 1689.

Petrou M, Clarke S, **Morrison K**, Bowles C, Dunn M and Yacoub M. (1999) Clenbuterol increases specific power and twitch speed of skeletal muscle for cardiac assist. Circulation
99: 713 - 720.

Ensminger SM, Witze O, Spriewald BM, **Morrison K**, Morris PJ, Rose ML and Wood KJ (2000). CD8+ T cells contribute to the development of transplant arteriosclerosis despite CD154 blockade. Transplantation 69: 2609 – 2612.

Ensminger SM, Spriewald BM, Witze O, **Morrison K**, Morris PJ, Rose ML and Wood KJ (2000). Intragraft IL-4 expression following CD154 blockade may trigger delayed development of transplant arteriosclerosis in the absence of CD8+ T cells. Transplantation 70: 955 - 963.

Raisky O, **Morrison KJM**, Obadia JF, McGregor J, Yacoub MH and Rose ML (2001). Acute rejection and cardiac graft vasculopathy in the absence of donor derived ICAM-1 or P-selectin. Journal of Heart and Lung Transplantation 20: 340 – 349.

Abusnara HJ, Smolenski RT, **Morrison K**, Yap J, Sheppard MN, O'Brien T, Suzuki K, Jayakumar J and Yacoub MH (2001). Efficacy of adenoviral gene transfer with manganese superoxide dismutase and endothelial nitric oxide synthase in reducing ischemia and reperfusion injury. European Journal of Cardiothoracic Surgery 20: 153 – 158.

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Misfeld M, **Morrison K**, Sievers H, Yacoub MH and Chester, AH (2002) Localization of immunoreactive endothelin and characterization of its receptors in aortic cusps. Journal of Heart Valve Disease 11: 472 - 476.

Weekes J, **Morrison K**, Mullen A, Wait R, Barton P and Dunn MJ (2003) Hyperubiquitination of proteins in dilated cardiomyopathy. Proteomics 3: 208 - 216.

Raisky O, Spriewald BM, **Morrison KJ**, Ensminger SM, Mohieddine T, Obadia JF, Yacoub MH and Rose ML (2003). CD8(+) T cells induce graft vascular occlusion in a CD40 knockout donr/recipient combination. Journal of Heart and Lung Transplantation 22: 177 - 183.

PATENTS:

EP1434592A4 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 121P2A3 USEFUL IN TREATMENT AND DETECTION OF CANCER

EP1409710A4 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 161P5C5 USEFUL IN TREATMENT AND DETECTION OF CANCER

EP1383922A4 NUCLEID ACID AND CORRESPONDING PROTEIN ENTITLED 158P3D2 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02083917C1 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 161P5C5 USEFUL IN TREATMENT AND DETECTION OF CANCER

EP1434592A1 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 121P2A3 USEFUL IN TREATMENT AND DETECTION OF CANCER

EP1409710A1 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 161P5C5 USEFUL IN TREATMENT AND DETECTION OF CANCER

EP1383922A2 NUCLEID ACID AND CORRESPONDING PROTEIN ENTITLED 158P3D2 USEFUL IN TREATMENT AND DETECTION OF CANCER

EP1372719A2 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 125P5C8 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02083068C1 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 121P2A3 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02083928A3 NUCLEID ACID AND CORRESPONDING PROTEIN ENTITLED 158P3D2 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02083928A2 NUCLEID ACID AND CORRESPONDING PROTEIN ENTITLED 158P3D2 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02083921A2 NULEIC ACIDS AND CORRESPONDING PROTEINS USEFUL IN THE DETECTION AND TREATMENT OF VARIOUS CANCERS

WO02083919A2 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 184P1E2 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02083917A2 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 161P5C5 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02083916A2 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 162P1E6 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02083860A2 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 151P3D4 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02083068A2 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 121P2A3 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02072785A3 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 125P5C8 USEFUL IN TREATMENT AND DETECTION OF CANCER

WO02072785A2 NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 125P5C8 USEFUL IN TREATMENT AND DETECTION OF CANCER

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CA2440461AA NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 161P5C5 USEFUL IN TREATMENT AND DETECTION OF CANCER

CA2440658AA NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED 125P5C8 USEFUL IN TREATMENT AND DETECTION OF CANCER